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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,677	04/15/2005	Margaret Forney Prescott	PA/4-32723A	1716

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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
KUDLA, JOSEPH S	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
09/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,677	PRESCOTT, MARGARET FORNEY	
	Examiner	Art Unit	
	JOSEPH S. KUDLA	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Foreword

1. Applicants' Amendment-After Non-Final Rejection, Information Disclosure Statement, amended claim set and amended specification, filed June 26, 2008, are acknowledged. With respect to Applicants' Arguments/Remarks in the correspondence, the arguments and request for reconsideration have been fully considered and are found to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objection are newly applied. They constitute the complete set presently applied to the instant specification. This action is **NON-FINAL**.

Instant claim 1 is amended and instant claim 18 is cancelled by Applicants' Amendment.

Instant claims 1 and 9 are presented for examination on the merits as they read upon the elected subject matter.

Information Disclosure Statement

2. The information disclosure statement filed June 26, 2008 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specifically, the references for DC and DD cited on Applicant's Form PTO-1449 have not been provided, therefore, the references have not been considered as to the merits of the case.

Claim Rejections - 35 USC § 103

(New Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Ross ("Atherosclerosis-An Inflammatory Disease," 1999, New Eng. J. Med., Volume 340, Pages 115-126)**, in view of **Jordan et al. (US Patent 7,090,865)**.

The instant invention claims a method of treating atherosclerosis in a patient via the administration of zoledronic acid. The instant invention also claims the bisphosphonate can be administered locally.

Ross teaches that atherosclerosis is an inflammatory disease (page 115, column 1, first sentence) which is hypothesized to occur due to endothelial denudation or dysfunction that if left unabated will result in the formation of an advanced, complicated lesion. Ross teaches causes of endothelial dysfunction includes elevated and modified LDL, diabetes, hypertension *inter alia* (page 115, column 2, paragraph 1). Ross teaches the endothelial dysfunction injury results in the increase of adhesiveness of the endothelium, increase in endothelial permeability and induces an inflammatory response which is mediated by monocyte-derived macrophages at every stage of the disease (page 115, column 2, second paragraph). Ross teaches that oxidation of LDL and internalization within macrophages leads to the formation of lipid peroxides and facilitates the formation of cholesterol esters which result in the formation of foam cells (page 116, column 1, paragraph 2).

Ross does not teach that zoledronic acid is capable of treating atherosclerosis.

Jordan et al. teach the delivery of a bisphosphonate into a macrophage causes apoptosis of the macrophage. Jordan et al. teach that a preferred bisphosphonate is zoledronic acid (column 7, lines 23-37). Jordan et al. teach that the bisphosphonate is administered to humans (column 15, lines 45-48).

It would have been obvious to one of ordinary skill in the art at the time of the invention that since arterial macrophages play a key role in the phagocytosis of oxidized LDL which are transformed into atherogenic foam cells, that any drug which inactivates or kills macrophages will inhibit foam cell formation and accumulation of atherosclerotic cholesterol in the artery. One of ordinary skill in the art would have been motivated to

utilize zoledronic acid to treat atherosclerosis due to its ability to cause apoptosis of macrophages and would have had a reasonable expectation of success due to the teachings of the prior art. Therefore, instant claim 1 is rendered obvious.

4. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Ross ("Atherosclerosis-An Inflammatory Disease," 1999, New Eng. J. Med., Volume 340, Pages 115-126**) and **Jordan et al. (US Patent 7,090,865)** as applied to claim 1 above, and further in view of **Duggan (WIPO Application Publication WO98/31359)**

The instant invention claims a method of treating atherosclerosis in a patient via the administration of zoledronic acid. The instant invention also claims the bisphosphonate can be administered locally.

Ross teaches that Atherosclerosis is an inflammatory disease (page 115, column 1, first sentence) which is hypothesized to occur due to endothelial denudation or dysfunction that if left unabated will result in the formation of an advanced, complicated lesion. Ross teaches causes of endothelial dysfunction includes elevated and modified LDL, diabetes, hypertension *inter alia* (page 115, column 2, paragraph 1). Ross teaches the endothelial dysfunction injury results in the increase of adhesiveness of the endothelium, increase in endothelial permeability and induces an inflammatory response which is mediated by monocyte-derived macrophages at every stage of the disease (page 115, column 2, second paragraph). Ross teaches that oxidation of LDL and internalization within macrophages leads to the formation of lipid peroxides and

facilitates the formation of cholesterol esters which result in the formation of foam cells (page 116, column 1, paragraph 2).

Jordan et al. teach the delivery of a bisphosphonate into a macrophage causes apoptosis of the macrophage. Jordan et al. teach that a preferred bisphosphonate is zoledronic acid (column 7, lines 23-37). Jordan et al. teach that the bisphosphonate is administered to humans (column 15, lines 45-48).

See the 35 USC 103 rejection at 3 for the rejection of instant claim 1.

Ross in view of Jordan et al. does not teach the local administration of zoledronic acid.

Duggan teaches the use of non-limiting bisphosphonate compounds useful for the treatment of atherosclerosis *inter alia* (page 3, lines 18-23 and page 26, line 7 to page 27, line 6) that can be delivered locally in the form of a liposome delivery system (page 29, lines 13-17).

It would have been obvious to one of ordinary skill in the art at the time of the invention that although Duggan does not each specifically mention the use of the bisphosphonate zoledronic acid, the phrase "non-limiting examples" of Duggan would have included all known bisphosphonates including zoledronic acid. It would have been obvious to one of ordinary skill in the art at the time of the invention that because Duggan teaches the administration of a bisphosphonate for the treatment of atherosclerosis via the same administration route, instant claim 9 is rendered obvious. One of ordinary skill in the art at the time of the invention would have been motivated to substitute zoledronic acid for those specifically listed in Duggan because of they are of

the same class of drug and, because of that, the local administration including zoledronic acid would have had a reasonable expectation of success.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JOSEPH S. KUDLA whose telephone number is (571)270-3288. The examiner can normally be reached on 9am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph S. Kudla/
Examiner, Art Unit 1611

September 22, 2008

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611